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Formulation And Evaluation Of Ketotifen Fumarate-Loaded Nanoparticles For Enhanced Transdermal Drug Delivery

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ABSTRACT

Ketotifen Fumarate, a non-competitive H1-receptor antagonist, is widely used for the prophylactic treatment of allergic conditions such as asthma, rhinitis, and chronic urticaria. However, its clinical effectiveness is limited by low oral bioavailability (~50%), short plasma half-life, and significant first-pass metabolism. This study aimed to overcome these limitations by formulating and evaluating lipid-based nanoparticles for potential transdermal delivery. Nanoparticles were prepared using soyalecithin and ethanol via the emulsification–solvent diffusion method, incorporating propylene glycol to enhance skin permeability. The formulations were characterized for particle size, zeta potential, encapsulation efficiency, swelling index, and in vitro drug release. Among the eight formulations (KFN-1 to KFN-8), KFN-6 showed optimal characteristics, including small particle size (93.47 µm), high zeta potential (27.16 mV), and encapsulation efficiency (89.38%). In vitro release studies indicated a sustained release profile, with Korsmeyer-Peppas kinetics suggesting a non-Fickian diffusion mechanism. The findings support the potential of lipid-based nanoparticles as an effective transdermal delivery system for improving the therapeutic performance of Ketotifen Fumarate

Keywords: Ketotifen Fumarate; Lipid-based nanoparticles; Transdermal drug delivery

1. INTRODUCTION

In the ever-evolving landscape of pharmaceutical sciences, nanotechnology has emerged as a powerful platform for enhancing drug delivery systems. Nanoparticles—submicron-sized colloidal systems ranging typically from 10 to 1000 nm—are particularly valuable for delivering poorly soluble, unstable, or rapidly metabolized drugs. Their ability to encapsulate therapeutic agents within a protective matrix can significantly improve bioavailability, provide sustained release, and target specific tissues, thereby minimizing systemic side effects and enhancing overall therapeutic efficacy. Ketotifen Fumarate is a benzocycloheptathiophene derivative that acts as a non-competitive H1-receptor antagonist and mast cell stabilizer. It is primarily indicated for the prophylactic treatment of bronchial asthma, allergic rhinitis, conjunctivitis, and chronic urticaria. While Ketotifen has shown effectiveness in mitigating allergic responses, its therapeutic potential is often compromised due to pharmacokinetic limitations. These include low oral bioavailability (~50%) due to significant first-pass hepatic metabolism, short plasma half-life (2–5 hours), and frequent dosing requirements, all of which can reduce patient compliance and therapeutic efficacy.

In the ever-evolving landscape of pharmaceutical sciences, nanotechnology has emerged as a powerful platform for enhancing drug delivery systems. Nanoparticles submicron-sized colloidal systems typically ranging from 10 to 1000 nm are particularly valuable for delivering poorly soluble, unstable, or rapidly metabolized drugs (Kohane, 2007; Sahoo et al., 2007). Their ability to encapsulate therapeutic agents within a protective matrix can significantly improve bioavailability; provide sustained release, and target specific tissues, thereby minimizing systemic side effects and enhancing overall therapeutic efficacy (Fang et al., 2009).Ketotifen Fumarate is a benzocycloheptathiophene derivative that acts as a non-competitive H1-receptor antagonist and mast cell stabilizer. It is primarily indicated for the prophylactic treatment of bronchial asthma, allergic rhinitis, conjunctivitis, and chronic urticaria (Khalil et al., 2001). While Ketotifen has shown effectiveness in mitigating allergic responses, its therapeutic potential is often compromised due to pharmacokinetic limitations, including low oral bioavailability (~50%) due to first-pass metabolism, a short plasma half-life (2–5 hours), and frequent dosing requirements—all of which may affect patient compliance and therapeutic efficacy (Fawaz et al., 2004)

To address these limitations, nanoparticle-based drug delivery systems offer a promising alternative. Nanoparticles can encapsulate Ketotifen Fumarate, protect it from degradation, prolong its release, and potentially bypass first-pass metabolism when administered through alternative routes such as transdermal delivery (Prausnitz & Langer, 2008). The transdermal route is non-invasive, bypasses hepatic metabolism, and offers sustained drug release, leading to stable plasma drug concentrations and improved patient adherence (Guy, 2010).

In the present study, nanoparticles were formulated using soyalecithin as the lipid matrix and ethanol as the organic solvent. These lipidic nanoparticles were designed to entrap Ketotifen Fumarate within their hydrophobic core, forming a stable colloidal dispersion when added to an aqueous phase under controlled stirring and temperature conditions. Propylene glycol was incorporated to enhance skin permeability and stabilize the nanoparticulate system (Verma & Pathak, 2010). The choice of lipid and solvent was guided by biocompatibility, drug-lipid solubility, and regulatory acceptability.

Nanoparticle-based drug delivery systems have gained significant attention for improving the therapeutic efficacy of drugs with poor bioavailability. **Kumar et al. (2016)** reported that lipid-based nanoparticles enhance the solubility and stability of lipophilic drugs, offering sustained release and improved absorption. **Dave et al. (2010)** demonstrated successful encapsulation of Ketotifen Fumarate in vesicular systems, showing improved drug retention and release profiles.

Mohammed et al. (2014) prepared and evaluated Ketotifen-loaded nanoparticles, reporting a significant increase in drug entrapment efficiency and extended drug release. Their findings indicated the suitability of nanoparticles for bypassing first-pass metabolism. **Patel et al. (2018)** explored the transdermal potential of Ketotifen using nanocarrier systems and observed enhanced permeability and therapeutic effect.

Furthermore, **Rao and Shirsand (2020)** emphasized that nanoformulations improve skin penetration due to their small particle size and increased surface area. These findings support the rationale for using lipid-based nanoparticles in transdermal drug delivery, especially for drugs like Ketotifen Fumarate, which suffer from limited oral bioavailability. The ultimate goal of this research is to develop a biocompatible, stable, and effective nanoparticulate drug delivery system for Ketotifen Fumarate that addresses the limitations of conventional oral formulations and improves therapeutic outcomes through controlled transdermal delivery.

2. Methodology

Materials

The materials used in this study included Ketotifen Fumarate as the active pharmaceutical ingredient, along with various excipients such as soya lecithin, propylene glycol, Tween 80, Span 60, Carbopol 934, triethanolamine, glycerol, methyl paraben, PEG 400, and sodium carboxymethyl cellulose. Solvents like methanol, ethanol, chloroform, and dichloromethane were used, alongside reagents including hydrochloric acid, sulphuric acid, sodium hydroxide, ferric chloride solution, aluminium sulphate, and sodium bicarbonate. Phosphate buffer saline (pH 7.4) and distilled water were prepared in the laboratory. All chemicals and reagents used were of analytical grade and sourced from reputable suppliers such as Merck, Loba Chemie, HiMedia, and SRL.

Table 2.1 Drug Profile: Ketotifen Fumarate

Parameter	Details
Drug Name	Ketotifen Fumarate
Chemical Name	1-[2-(4-Phenylthiazol-2-ylthio)ethyl]-4-piperidyl fumarate
Molecular Formula	C19H19N3O2S2
Molecular Weight	383.51 g/mol
CAS Number	34580-14-8
Mechanism of Action	H1 receptor antagonist and mast cell stabilizer; inhibits histamine release
Indications	1. Bronchial asthma (prophylaxis) 2. Allergic rhinitis 3. Allergic conjunctivitis 4. Skin allergies (e.g., urticaria)

Pharmacokinetics	Absorption: Well absorbed orally Bioavailability: ~50% Tmax: 2–3 hours Metabolism: Hepatic Half-life: ~12 hours Excretion: Urine
Dosage Forms	Tablets (1 mg), Syrup (pediatric), Eye drops (0.025%)
Side Effects	Common: Drowsiness, dry mouth, headache Less common: Nausea, weight gain Serious: Rare arrhythmias, blood dyscrasias
Contraindications	Hypersensitivity, children <3 yrs (oral), caution in liver disease or seizures
Drug Interactions	CNS depressants, other antihistamines, CYP3A4 inhibitors
Precautions	Avoid driving, monitor allergic reactions, discontinue on serious side effects
Storage	Cool, dry place; protect tablets from moisture and light
Pharmacological Class	Antihistamine (H1 antagonist), Mast cell stabilizer

2.2 Identification of drug ketotifen fumarate

2.2.1 Melting point method (Capillary Tube Method):

A small, finely powdered sample of Ketotifen Fumarate is packed into a capillary tube and placed in a melting point apparatus. The sample is heated gradually (1–2°C/min), and the temperature at which it completely liquefies is recorded as the melting point. The procedure is repeated for accuracy..

2.2.2 Solubility

100 mg of Ketotifen Fumarate is mixed with a measured solvent volume, stirred until fully dissolved, and the temperature is noted. Solubility is calculated as drug mass (g) divided by solvent volume (mL), expressed in g/mL.

2.2.3 Partition coefficient

A known amount of Ketotifen Fumarate is mixed with equal volumes of water and organic solvent, shaken to equilibrium, and the drug concentration in each phase is measured. The partition coefficient (K) is calculated as C_1/C_2, indicating lipophilicity and membrane permeability.

2.2.4 Loss on Drying

Determination of flow properties of pure drug

A weighed Ketotifen Fumarate sample is heated at 105°C, and the weight loss after drying is measured. LOD (%) is calculated as:

[(Initial weight – Final weight) / Initial weight] × 100

2.2.5 Bulk density

Bulk density (g/mL) is determined by placing sieved Ketotifen Fumarate into a 100 mL cylinder without tapping. It's calculated as:

Bulk density = Mass of powder / Volume occupied.

2.2.6 Tapped density

Tapped density is calculated by mechanically tapping a powder-filled cylinder until volume stabilizes. It's given by:

Tapped density = Mass of powder / Tapped volume, indicating powder compactness and flow properties.

2.2.7 Compressibility index and Hausner ratio

Carr's Index and Hausner Ratio assess powder flowability.

Carr's Index = (TD − BD) / TD × 100

Hausner Ratio = TD / BD.

Lower values (CI < 15%, HR ≤ 1.25) indicate good flow; higher values suggest poor flow due to stronger interparticle interactions.

Table 2.2 Carr's index standard value

S. no.	Carr's index	Flow character
1.	5-15	Excellent
2.	12-16	Good
3.	18-21	Fair to passable
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Very very poor

2.2.8 Angle of repose

Angle of repose indicates powder flowability. It's the angle formed by a powder heap on a flat surface. Higher angles mean poor flow; lower angles suggest better flow. It's calculated as $\theta = \tan^{-1}(h/r)$, where h is pile height and r is base radius. Glidants can reduce the angle, improving flow up to a limit.

Table 2.3 Standard value of angle of repose

Angle of repose(θ)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

2.3 Ketotifen Fumarate loaded nanoparticles

Ketotifen Fumarate and soyalecithin are dissolved in ethanol, mixed with propylene glycol (organic phase), and added to warm distilled water (aqueous phase) under high-speed stirring to form an emulsion. As ethanol evaporates, nanoparticles form. These are collected by centrifugation, washed, and dried for storage.

Table 2.4 Composition of Ketotifen Fumarate loaded nanoparticles

S.No	Formulation Code	Ketotifen Fumarate (%w/w)	Soyalecithin (%w/w)	Ethanol (%w/w)	Propylene glycol (%w/w)	Water
1.	KFN-1	2	2	40	1	Q.S
2.	KFN-2	2	3	20	1.25	Q.S
3.	KFN-3	2	4	30	1.5	Q.S
4.	KFN-4	2	2	30	1.25	Q.S
5.	KFN-5	2	3	40	1	Q.S

6.	KFN-6	2	4	20	1.5	Q.S
7.	KFN-7	2	2	20	1.25	Q.S
8.	KFN-8	2	3	30	1	Q.S

2.3 Characterization of nanoparticles

2.3.1Particle Size

Particle size of Ketotifen Fumarate-loaded nanoparticles is measured using Dynamic Light Scattering (DLS) after sonication. Results include average size (ideally <200 nm) and polydispersity index (PDI), ensuring uniformity, stability, and suitability for transdermal delivery.

2.3.2 Polydispersity index (PDI) and Zeta Potential

PDI indicates nanoparticle size uniformity; values <0.3 reflect a stable, monodispersed system ideal for drug delivery.

2.3.3 Zeta Potential

Zeta Potential reflects nanoparticle surface charge and stability. Values >±30 mV indicate strong repulsion and good stability. For Ketotifen Fumarate nanoparticles, a high absolute Zeta Potential and low PDI ensure uniformity, prevent aggregation, and support transdermal delivery effectiveness.

2.3.4 % Encapsulation Efficiency

To assess the total drug encapsulated in Ketotifen Fumarate-loaded nanoparticles, a known amount of formulation was centrifuged at 14,000 rpm for 15 minutes at 4°C using an ultracentrifuge. The supernatant was collected and analyzed at 272 nm using a UV-visible spectrophotometer (Dave et al., 2010; Mohammed et al., 2014). Entrapment efficiency was calculated using the formula:

% Entrapment Efficiency = (Amount of drug in nanoparticles / Total drug added) × 100

3. RESULTS & DISCUSSIONS

3.1 Preformulation studies:

Preformulation studies are essential in drug development to understand the physical and chemical properties of a drug and optimize its formulation.

3.2 Organoleptic properties

White to off-white crystalline powder with a smooth, fine texture; odorless with a characteristic bitter taste.

Table 3.1 The organoleptic properties of ketotifen fumarate

S.No	Properties	Outcome	Description
1	Colour	White to off-white	Typical appearance
2	Shape	Crystalline	Fine crystalline particles
3	Odour	Odorless	No noticeable smell
4	Texture	Powdery	Smooth and fine powder
5	Taste	Bitter	Characteristic bitterness

3.1 Identification of Ketotifen fumarate

3.1.1 Melting point

Approximately 193–197°C, indicating purity and aiding in determining appropriate processing and storage conditions.

Table 3.2 Melting point of Ketotifen fumarate

Crude drug	Melting point
Ketotifen fumarate	193-197°C

3.2 Solubility of Ketotifen fumarate

Ketotifen Fumarate exhibits varying solubility in different solvents. In ethanol, it is slightly soluble, forming a slightly hazy solution. In petroleum ether, it is insoluble, showing no visible dissolution. When tested in water, Ketotifen Fumarate is slightly soluble, with minimal dissolution observed. In methanol, it is soluble, forming a clear solution. The solubility in acetone is also good, resulting in a clear solution. Finally, in chloroform, Ketotifen Fumarate is very slightly soluble, with only faint dissolution observed.

Table 3.3 Solubility of Ketotifen fumarate in different solvents

S.No	Parameters (% w/w)	Solubility	Observation
1	Ethanol	Slightly soluble	Forms a slightly hazy solution
2	Petroleum Ether	Insoluble	No visible dissolution
3	Water	Slightly soluble	Minimal dissolution observed
4	Methanol	Soluble	Clear solution
5	Ethanol (repeat)	Slightly soluble	Similar slight dissolution observed
6	Acetone	Soluble	Clear solution
7	Chloroform	Very slightly soluble	Faint dissolution observed

3.3 UV Spectrum

The UV spectrum of Ketotifen Fumarate typically shows absorption peaks in the UV-visible range, often around 220-230 nm. This range corresponds to the aromatic rings and conjugated systems in the structure of Ketotifen Fumarate, which absorb UV light. The exact peaks may vary depending on the solvent and concentration used for the analysis. The UV spectrum of Ketotifen fumarate is shown in figure.

3.4 Loss on drying of Ketotifen fumarate

The Loss on Drying for Ketotifen Fumarate is 11.25% w/w, indicating that 11.25% of the drug's weight is lost when subjected to drying. The value is shown in table 5.4.

Table 3.4 Loss on drying

Crude drug	Loss on drying (% w/w)*
Ketotifen fumarate	11.25

3.5 Preparation of standard curve of Ketotifen fumarate

3.5.1 Preparation of Phosphates buffer pH 7.4 Ketotifen fumarate

The **phosphate buffer (pH 7.4)** is used to maintain a stable medium for Ketotifen Fumarate's solubility and absorption. A standard solution prepared in this buffer exhibits a **linear increase in absorbance with increasing concentration**, confirming **Beer-Lambert's law**.

Table 3.5 Absorbance of working standard solution

S. No.	Concentration (µg/ml)	Absorbance at λ nm
1.	0	0.0934
2.	2	0.1256
3.	5	0.1578
4.	10	0.1900
5.	12	0.2222
6.	15	0.2544
7.	25	0.2866

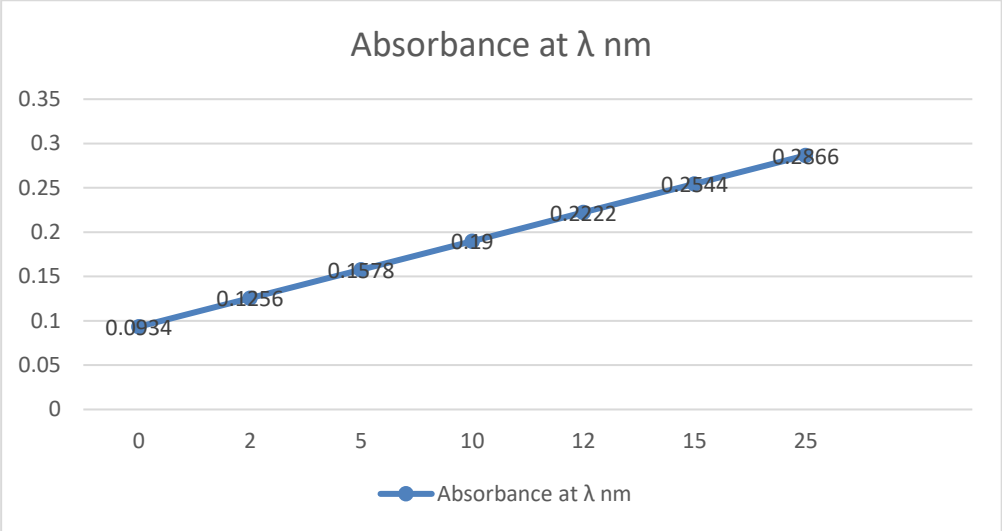


Figure 3.1 Graph of Phosphates buffer pH 7.4 Ketotifen fumarate

3.6 Preparation of standard curve of Ketotifen fumarate in Water

The absorbance of the working standard solution of **Ketotifen Fumarate in water** demonstrates a clear linear relationship with concentration, indicating reliable results for quantitative analysis. At **0 µg/ml**, the absorbance is **0.0512**, serving as the baseline measurement. As the concentration increases, so does the absorbance. At **2 µg/ml**, the absorbance is **0.1276**, and at **5 µg/ml**, it reaches **0.192**. This trend continues with **0.2464** at **10 µg/ml** and **0.2964** at **12 µg/ml**. As the concentration increases further, the absorbance values are **0.3581** at **15 µg/ml** and **0.4174** at **25 µg/ml**. The consistent increase in absorbance with concentration is indicative of good linearity, which is a key feature for accurate analysis. This data confirms the suitability of this concentration range for determining the concentration of Ketotifen Fumarate using UV-Vis spectrophotometry, following the Beer-Lambert law, and ensuring precise quantification in further studies.

Table 3.6 Absorbance of working standard solution (Ketotifen fumarate in Water)

S. No	Concentration (µg/ml)	Absorbance λmax

1.	**0**	0.0512
2.	**2**	0.1276
3.	**5**	0.192
4.	**10**	0.2464
5.	**12**	0.2964
6.	**15**	0.3581
7.	**25**	0.4174

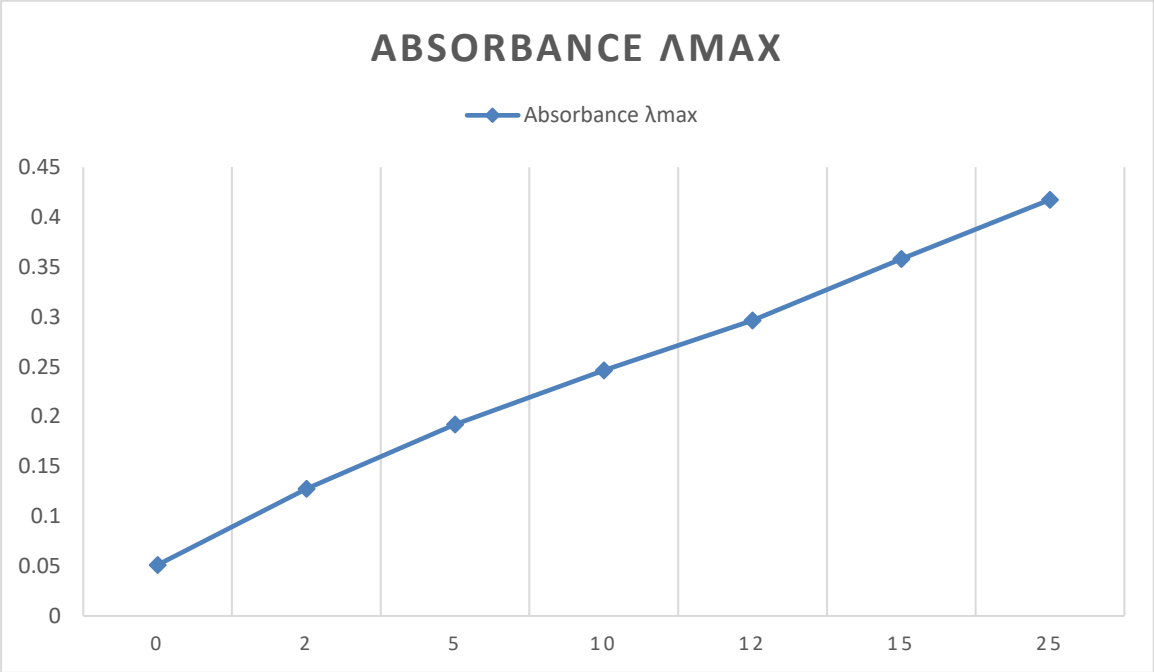


Figure 3.2 Graph of standard curve of Ketotifen fumarate in water

3.6.1 Preparation of standard curve for drug loading study in ethanol

The standard curve for Ketotifen Fumarate in ethanol showed a linear increase in absorbance with rising concentration. Absorbance values were: 0 µg/ml – 0.000, 2 µg/ml – 0.110, 5 µg/ml – 0.200, 10 µg/ml – 0.299, and 15 µg/ml – 0.410, confirming a direct relationship between concentration and absorbance.

Table 3.7 Absorbance of working standard solution

S.no	Concentration (µg/ml)	Absorbance
1.	**0**	**0**
2.	**2**	**0.110**

3.	**5**	**0.200**
4.	**10**	**0.299**
5.	**15**	**0.410**

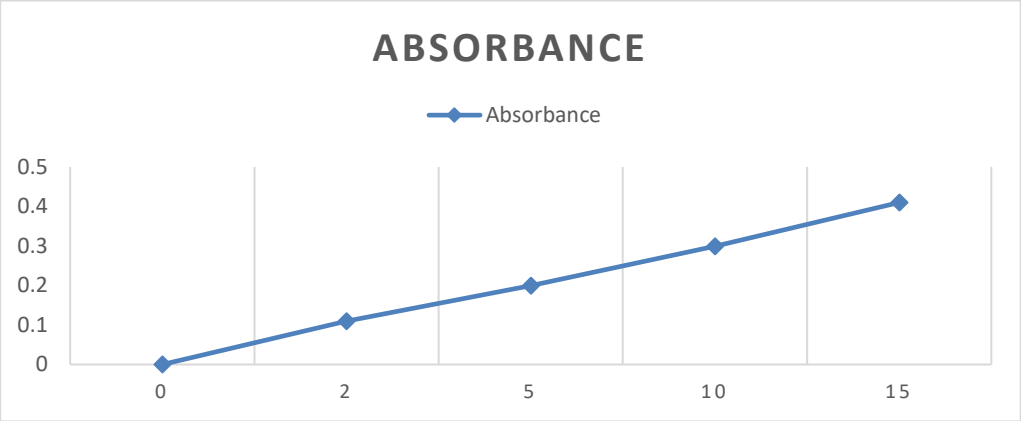


Figure 3.3 Graph of standard curve for drug loading

3.7 Determination of flow properties of pure drug

3.7.1 Bulk density and tapped density

The flow properties of the pure drug were determined by measuring the bulk density. The bulk density of the pure drug was found to be 0.54 g/cm³. This value provides insight into the powder's packing ability and is essential for evaluating the flowability of the drug during formulation processes. The values are shown in table and illustrated in figure.

Table 3.8 Determination of flow properties of pure drug

Parameters	Values
Bulk density	0.54
Tapped density	0.606

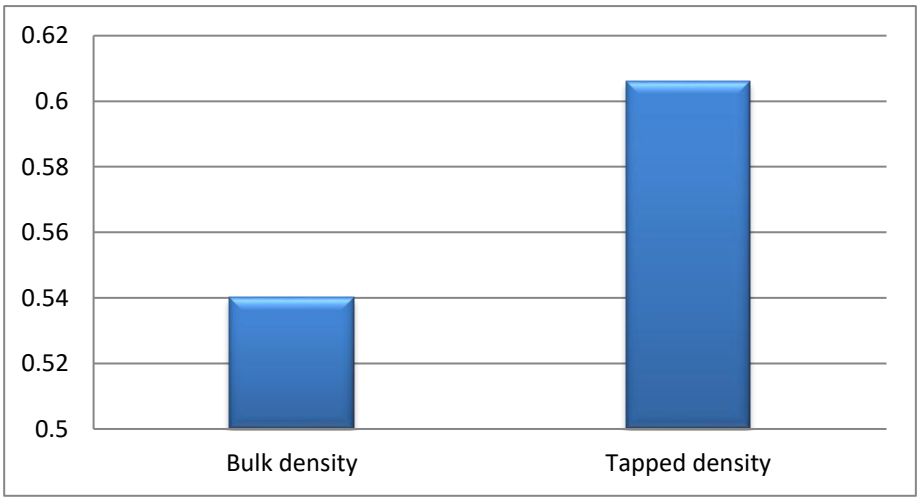


Figure 3.4 Graph of flow properties of Ketotifen fumarate

3.7.2 Compressibility index, hausner ration and angle of repose

The flow properties of Ketotifen Fumarate indicate good suitability for formulation. The Compressibility Index was 10.9%, Hausner Ratio 1.12, and Angle of Repose 27.26°, all suggesting acceptable to good flow characteristics ideal for processing.

Table 3.9 Compressibility index, hausner ration and angle of repose

Parameters	Values
Compressibility index (%)	10.9%
Hausner ratio	1.12
Angle of repose	27.26^0

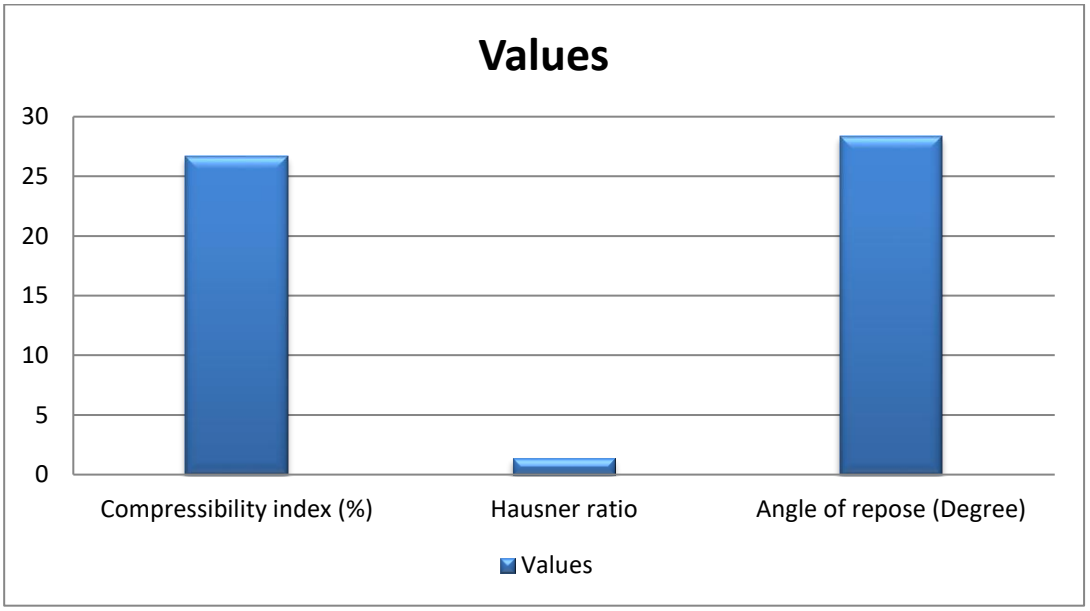


Figure 3.5 Graph of flow properties of Ketotifen fumarate

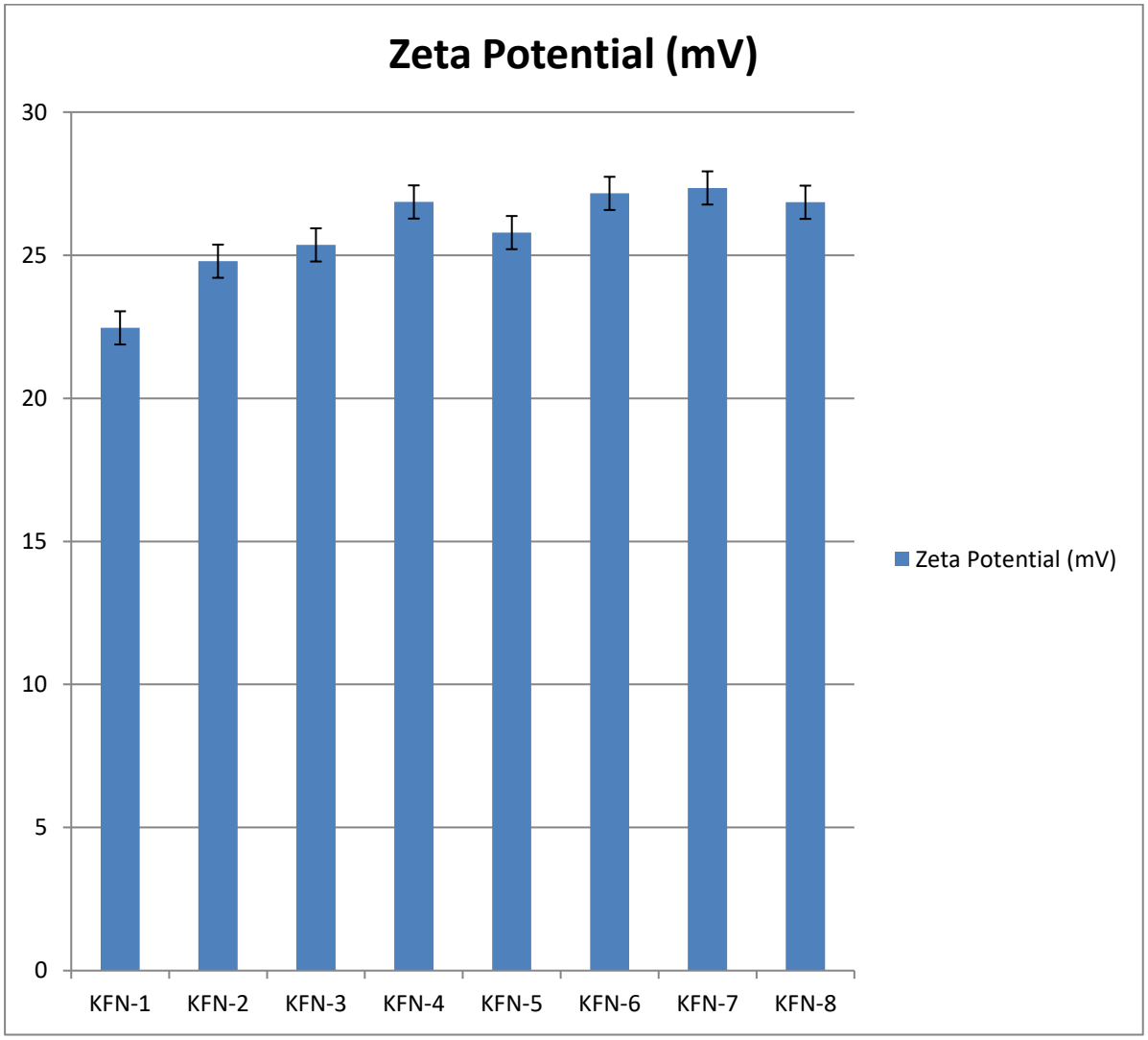
3.7.3 Characterization of Ketotifen fumarate nanoparticles

The evaluation of Ketotifen Fumarate nanoparticle formulations (KFN) showed variability in zeta potential, particle size, and yield. Among all, KFN-6 demonstrated the most favorable characteristics with the highest zeta potential (27.16 mV), smallest particle size (93.47 µm), and a high yield (90.51%), indicating excellent stability, efficient drug delivery potential, and formulation efficiency. In contrast, KFN-8 had the largest particle size (181.62 µm), while KFN-4 showed the lowest yield (64.95%). Overall, KFN-6 emerged as the most promising formulation.

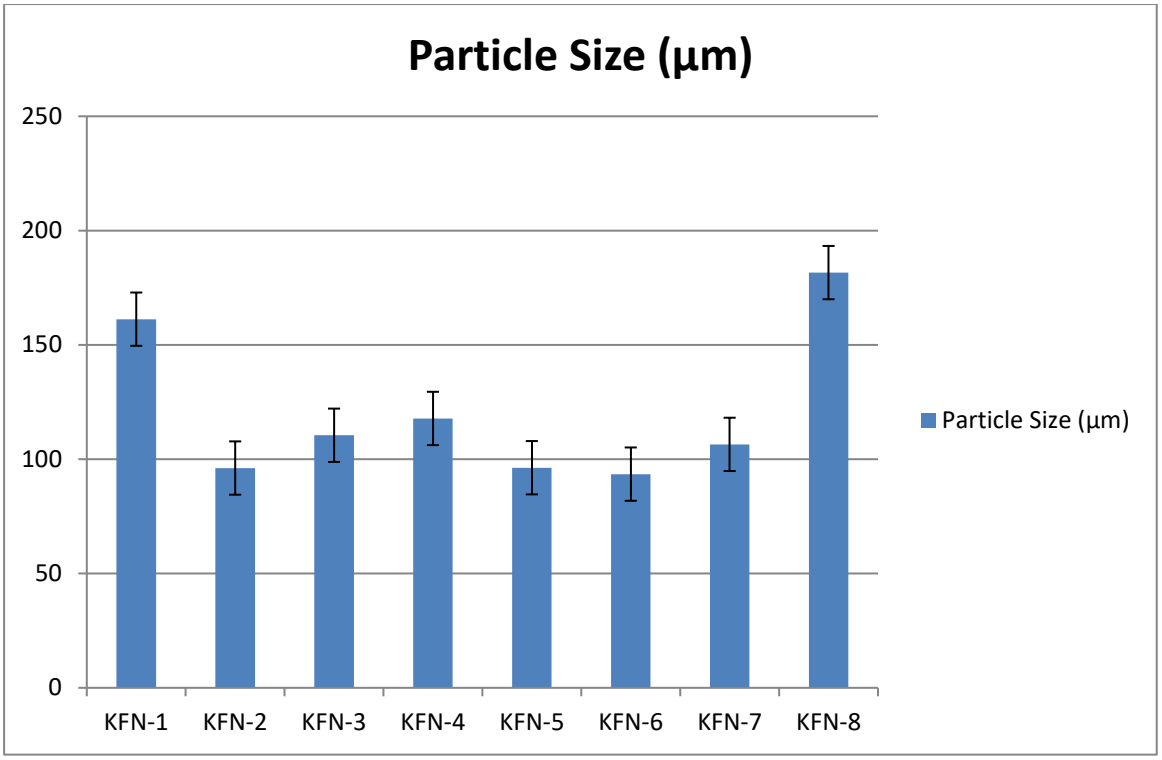
Table 3.10 Evaluation of different formulations of nanoparticles

Formulation (Nanoparticles - KFN)	Zeta Potential (mV)	Particle Size (µm)	Yield Percentage (%)
KFN-1	22.46	161.25	92.87
KFN-2	24.79	96.13	74.49

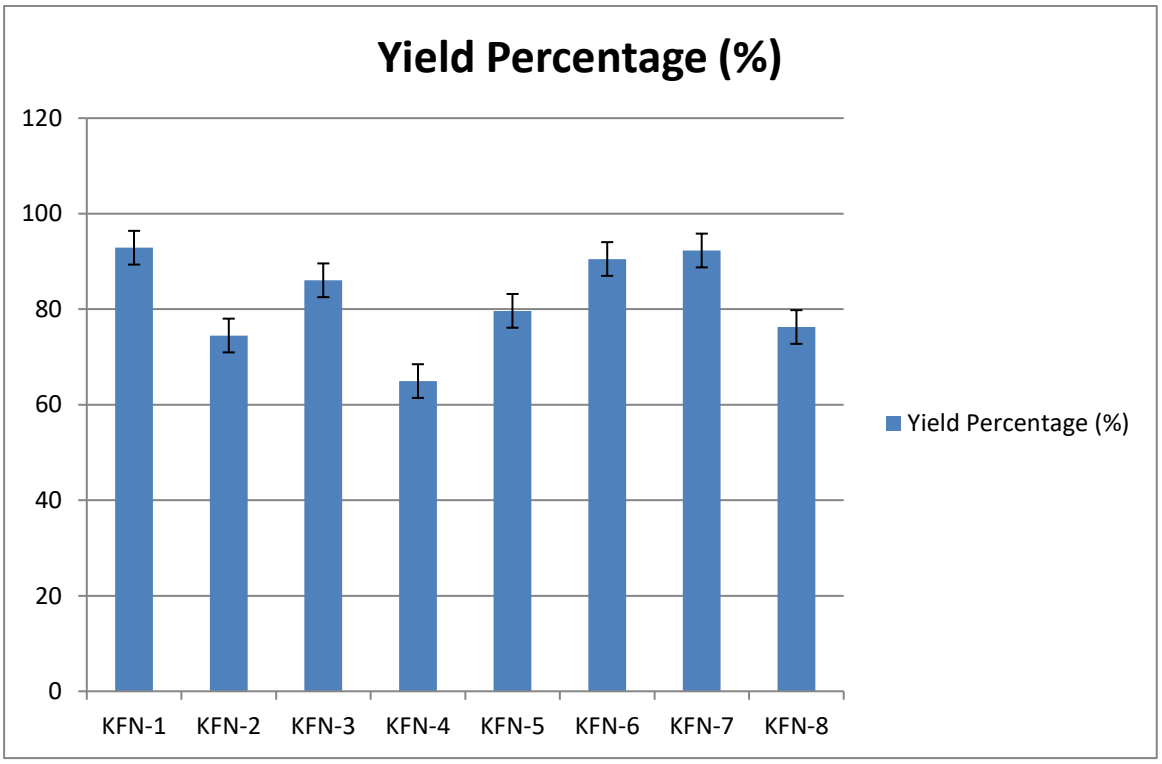
KFN-3	25.36	110.47	86.05
KFN-4	26.86	117.82	64.95
KFN-5	25.79	96.27	79.65
KFN-6	27.16	93.47	90.51
KFN-7	27.35	106.49	92.29
KFN-8	26.85	181.62	76.27



Graph 3.1: Evaluation of different formulations for Zeta potential (mv)



Graph 3.2: Evaluation of different formulations for Particle size (µm)



Graph 3.3: Evaluation of different formulations for Yield Percentage (%)

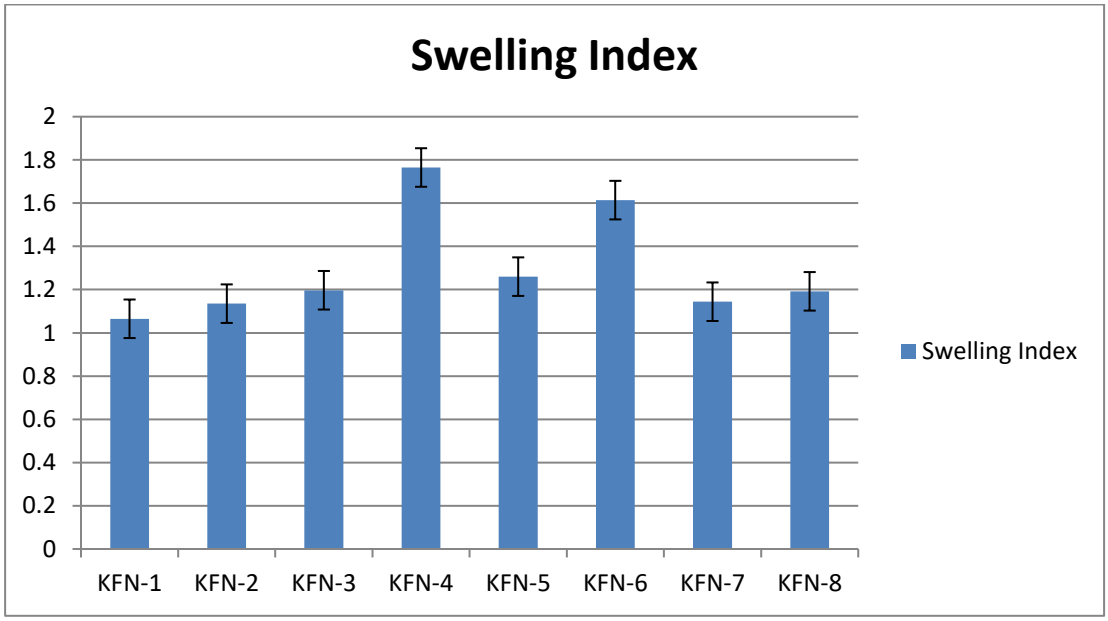
3.8 Evaluation of different formulations of naonoparticles

The nanoparticle formulations of Ketotifen Fumarate showed variation in Swelling Index and % Encapsulation Efficiency. KFN-4 had the highest swelling (1.765), while KFN-1 had the lowest (1.065). Encapsulation efficiency ranged from 81.51% (KFN-1) to 90.84% (KFN-7). KFN-6 showed a good balance between both parameters, making it a promising formulation

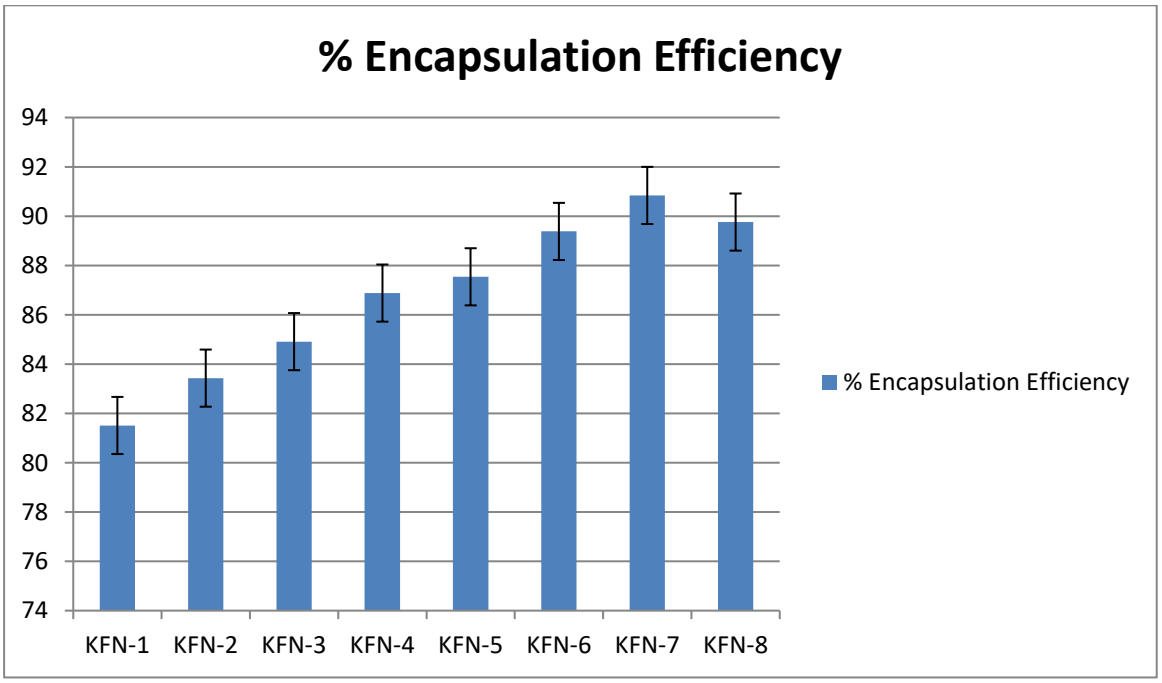
for further study.

Table 3.11 Evaluation of different formulations of naonoparticles

Formulation Code	Swelling Index	% Encapsulation Efficiency	Remarks
KFN-1	1.065 (Lowest)	81.51% (Lowest)	Lowest values observed
KFN-4	1.765 (Highest)	86.88%	Highest swelling index
KFN-6	1.614	89.38%	Balanced & promising formulation
KFN-7	1.144	90.84% (Highest)	Highest encapsulation efficiency



Graph 3.4: Evaluation of different formulations of naonoparticles (Swelling Index)



Graph 3.5: Evaluation of different formulations of naonoparticles (% Encapsulation Efficiency)

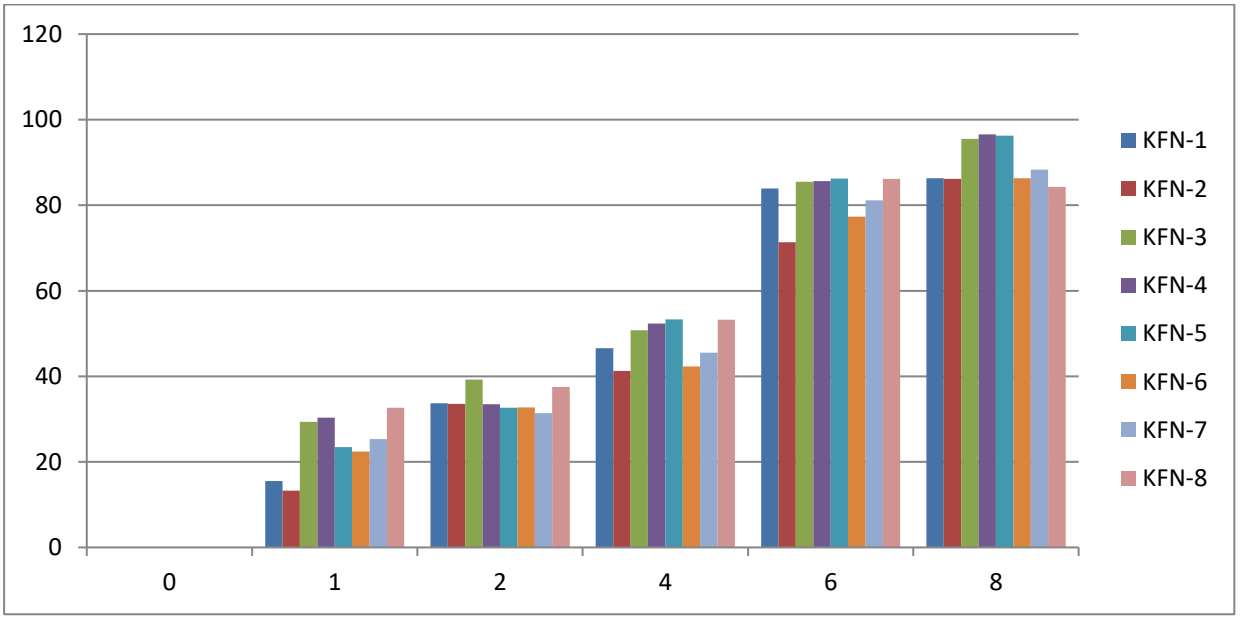
3.9 Cumulative percentage release of naonoparticles in phosphate buffer pH 7.4.

The cumulative drug release of Ketotifen Fumarate nanoparticles varied across formulations. At 1 hour, release ranged from 13.26% (KFN-2) to 32.63% (KFN-8). By 4 hours, KFN-5 and KFN-4 showed the highest release (53.34% and 52.32%), while KFN-2 remained lowest. At 8 hours, KFN-4 and KFN-5 reached the highest release (96.52% and 96.25%), whereas KFN-8 and KFN-2 had the lowest (84.3% and 85.3%). This indicates that KFN-4 and KFN-5 exhibited superior sustained release profiles.

Table 3.12 Cumulative percentage release

Time (h)	KFN-1	KFN-2	KFN-3	KFN-4	KFN-5	KFN-6	KFN-7	KFN-8
0	0	0	0	0	0	0	0	0
1	15.51	13.26	29.34	30.32	23.42	22.42	25.29	32.63
2	33.73	33.53	39.23	33.46	32.63	32.7	31.36	37.53
4	46.59	41.25	50.73	52.32	53.34	42.31	45.53	53.25
6	83.93	71.36	85.5	85.64	86.25	77.31	81.17	86.19
8	86.3	86.19	95.48	96.52	96.25	86.29	88.32	84.3

***Values are average of 3 readings ± S.D.**



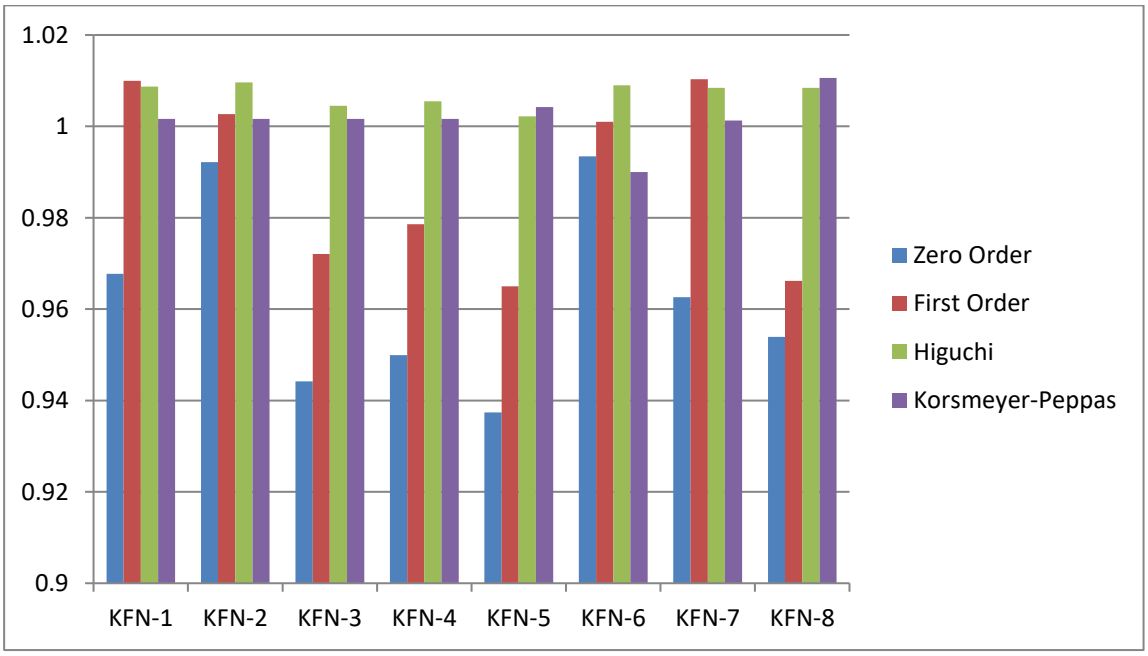
Graph 3.6: Cumulative percentage release of DRUG

3.9.1 Release kinetics

In vitro drug release of Ketotifen Fumarate nanoparticles (pH 7.4) best fit the Korsmeyer-Peppas model, indicating non-Fickian (diffusion + erosion) release. Formulations KFN-2, KFN-6, and KFN-7 also fit the Higuchi model, suggesting diffusion-controlled release. Overall, drug release was governed by a combination of mechanisms.

Table 3.13 Results of curve fitting of the in vitro drug release data from naonoparticles in phosphate buffer (pH 7.4)

Batch Code	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
KFN-1	0.9677	1.0100	1.0087	1.0016
KFN-2	0.9922	1.0027	1.0096	1.0016
KFN-3	0.9442	0.9721	1.0045	1.0016
KFN-4	0.9499	0.9786	1.0055	1.0016
KFN-5	0.9374	0.9650	1.0022	1.0042
KFN-6	0.9934	1.0010	1.0090	0.9900
KFN-7	0.9626	1.0103	1.0084	1.0013
KFN-8	0.9539	0.9662	1.0084	1.0106



Graph 7: Results of curve fitting of the in vitro drug release data from Nanoparticles in phosphate buffer (pH 7.4)

4. CONCLUSIONS

The present study successfully demonstrated the development and evaluation of Ketotifen Fumarate-loaded lipid-based nanoparticles as a potential transdermal drug delivery system. The formulated nanoparticles exhibited favorable physicochemical properties including optimal particle size, high zeta potential, good entrapment efficiency, and sustained drug release profiles. Among all formulations, KFN-6 showed the best overall performance in terms of encapsulation efficiency, particle size, and stability, making it a promising candidate for further investigation. The in vitro release kinetics followed the Korsmeyer-Peppas model, indicating a non-Fickian diffusion mechanism, and the enhanced drug release suggests improved therapeutic potential. This nanoparticulate system may overcome the pharmacokinetic limitations associated with conventional oral formulations of Ketotifen Fumarate, offering improved patient compliance, prolonged drug action, and better management of allergic disorders.

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6. Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this research work.

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